REMARKS/ARGUMENTS

In response to the Non-Final Rejection mailed July 15, 2003, Applicants have amended Claims 5-10, added new claim 33 and present the following remarks.

In response to making the Restriction Requirement FINAL, applicants cancel the non-elected claims without prejudice to refilling them in one or more continuing or divisional applications.

To comply with certain informalities, the specification has been amended to include reference to the provisional patent application from which applicants claim priority. Also, a description of Figure 3 in the specification has been amended to correct a typographical error.

Claims 6, 8, and 10 were rejected under 35 USC 112, second paragraph as allegedly being indefinite. Specifically claims 6, 8 and 10 are objected to as reciting SEQ ID NO:1, which lists a DNA sequence in the RNA virus of claims 6, 8 and 10. The rejection is respectfully traversed because it is conventional to list RNA sequences in the scientific literature by their DNA equivalents. One of ordinary skill in the art knows this and would not be confused. Nonetheless, claims 6, 8 and 10 have been amended to avoid the language and any possible confusion.

Claims 5-10 were rejected under 35 USC 112, first paragraph as failing to comply with the written description requirement. Specifically, the examiner contends that no RNA plant viruses or RNA molecules are described with the claimed structural elements. This rejection is respectfully traversed.

The methodology for preparing RNA plant viruses and RNA molecules with all of the claimed features are described in the specification in several locations including page 10, line 20 to page 11 line 14, where the gene is inserted into a GENEWARE vector, Figure 2 provides the nucleotide sequence of the vector including the bovine lysozyme gene inserted therein, Figure 3 depicts the structural configuration and page 17 lines 22 to 27 even list the deposit information where an RNA plant virus containing the claimed RNA molecule and all of the claimed structural features was deposited in ATCC before the filing date of applicants' priority document. Evidence of the virus replicating and

expressing the bovine lysozyme gene are found on page 11, line 15 to page 17, line 16 and Example 2 and 3 with photographs and graphical data being shown in Figures 4 to 10. Accordingly, this rejection should be withdrawn.

Claims 5-10 were rejected under 35 USC 112, first paragraph as failing to comply with the enablement requirement. Specifically the examiner contends that it is unpredictable that any RNA produced from a DNA template would be the desired RNA, particularly since the specification provides no examples of such an RNA. This rejection is respectfully traversed.

While the examiner considers it unpredictable to obtain the desired RNA/virus from a DNA template, it should be noted that the prior art cited in the rejection below (Donson et al) prepared plant RNA viruses with a foreign gene from a DNA template in their Example 1. With the basic technology filed almost 10 years old, ago showing that a method for producing a desired RNA virus from a DNA template, it is unreasonable for the examiner to contend that that aspect of the present invention is unpredictable.

While there are some unpredictable aspects to the present invention and the technology associated with it, as will be discussed below, the basis for the rejection is not one of them. Furthermore, what the examiner contends is unpredictable was actually accomplished before the filing date of the present application by the inventors as shown by the specification examples. Past success negates any claim of unpredictability. Accordingly, the rejection should be withdrawn.

Claims 5 and 6 were rejected under 35 USC 102(b) as being anticipated by Mirkov et al. Reference is made to a section of various possible vectors for making a transgenic plant that may possibly be used to express bovine lysozyme. This rejection is respectfully traversed.

While the rejection refers to passages suggesting satellite tobacco mosaic virus as a possible vector for carrying a bovine lysozyme gene, there is no evidence that STMV is capable of doing so. The reference, nor any other, has not shown that STMV with a foreign gene insert is capable of packaging, replicating or expressing any foreign gene in vivo, much less bovine lysozyme. STMV is a very small satellite virus (1059 nucleotides, Kurath et al, Virology 202(2): 1065-9) and the rejection does not establish

that it is capable of packaging the extra lysozyme sequence and replicating with an insert such as bovine lysozyme (444 nucleotides not counting required regulatory sequences) and expressing the same. The disclosure is not enabling to teach anything which actually works.

Mirkov et al is interested in producing transgenic plants and the use of STMV is used in the context of developing transgenic plants. See column 12, lines 27-48. Indeed the only transgenic plants are shown in the examples and claims. Mirkov et al appears to be using STMV as a way of making transgenic plant. An integrating vector is not necessarily a virus that has a normal reproductive lifecycle. By contrast, the deposited virus of the present invention infects and reproduces more virus in the natural sense and does not integrate into the plant genome. Present claims 5 and 6 recite a "virus", not merely a RNA molecule or a polynucleotide vector. Accordingly, Mirkov et al does not teach the claimed invention.

Claims 5-10 were rejected under 35 USC 103(a) as being obvious over Mirkov et al taken in view of Donson et al. The examiner contends that Mirkov et al teaches a recombinant RNA plant virus having the bovine lysozyme gene. Donson et al is cited to teach the general construct of TMV viruses expressing various other genes in plants. The examiner contends that it would have been obvious to use the bovine lysozyme gene in a Donson et al vector system to express bovine lysozyme protein in plants. This rejection is respectfully traversed.

Not all recombinant foreign genes are capable of being expressed by a RNA plant virus. Even though Donson et al did express a foreign gene in plants using the TMV system, there is no indication that bovine lysozyme can be expressed using the same system. The fact that Mirkov et al disclose making a transgenic plant by integrating the bovine lysozyme gene into the plant genome does not ensure a predictable outcome.

In order for one to infect and replicate an RNA virus in a plant and for the foreign gene to be expressed, many events must occur, some of which are not predictable and are not suggested by anything in Mirkov et al or Donson et al. These include:

1) The recombinant virus with the lysozyme gene must be able to replicate in the plant cell.

2) The recombinant virus must retain the lysozyme sequence long enough to make the protein product.

3) The specific recombinant construct must be compatible with the host plant cell.

4) To infect a whole plant the recombinant virus must be able to move throughout the growing parts of the plant while retaining the lysozyme gene.

5) The viral capsids must be able to assemble to encompass both the viral genome and an additional lysozyme gene.

6) The lysozyme gene must be expressed and not degraded by the plant cell.

7) The expressed lysozyme protein must be retained by the plant sufficiently to protect it from bacterial infections.

8) Unlike vectors containing a lysozyme gene, infectious viruses must retain all of the other biological properties in order to infect a whole plant.

Neither Mirkov et al nor Donson et al provide a suggestion that any of these events are even possible with lysozyme, much less predictable. Thus the suggestion in Markov et al is not enabling. Viruses are generally very efficient organisms and have very limited ability to include additional gene(s). To add bovine lysozyme and minimal regulatory sequences to STMV would increase the satellite virus size by at least 50%. This alone provides doubt as to the operability of such a suggestion by Markov et al. The unpredictability of living organisms is much greater than laboratory constructs acting as little more than chemicals. Without reasonable predictability of successful results, one lacks motivation to make the claimed molecule or virus.

Mirkov et al does not establish that their transgenic plants are capable of producing biologically active bovine lysozyme protein. While their transgenic plants retain the bovine lysozyme gene (Example 4), the biological activity is based on that of the marker gene, kanamycin resistance. A bovine lysozyme protein may be produced in Example 5, but its presence is based an antibody binding to a band on a denatured (95 C in SDS for 4 minutes) electrophoresis gel. See column 29, lines 11-35. The process appears to denature whatever proteins are present and thus Mirkov et al does not show that a native, undenatured, biologically active lysozyme is ever made by the plant cells.

Recombinant host cells are notorious for denaturing the protein of any foreign gene, especially when from a similar source. Cattle and tobacco plants so unrelated that the species are in different kingdoms. Without actually testing the plant cells for the biological activity of lysozyme in a bacterial lysis assay or the like, one does not know whether biologically active native bovine lysozyme can ever be expressed in a plant.

Accordingly, the claims as written are not obvious over Mirkov et al in view of Donson et al and the rejection should be withdrawn.

In view of the above amendments and comments, the claims are now in conditions for allowance and applicants request a timely Notice of Allowance be issued in this application.

The commissioner hereby is authorized to charge payment of any fees under 37 CFR § 1.17, which may become due in connection with the instant application or credit any overpayment to Deposit Account No. 500933.

Respectfully submitted,

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